

WHAT IS CLAIMED IS:

1. An isolated variant allele of a human orphanin FQ/nociceptin receptor gene, comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof.
1. 2. The isolated variant allele of Claim 1, detectably labeled.
1. 3. The isolated variant allele of Claim 2, wherein said detectable label comprises a radioactive element, a chemical which fluoresces, or an enzyme.
1. 4. An isolated nucleic acid molecule selectively hybridizable to the isolated variant allele of Claim 1.
1. 5. The isolated nucleic acid molecule of Claim 4, detectably labeled.
1. 6. The isolated nucleic acid molecule of Claim 5, wherein said detectable label comprises a radioactive element, a chemical that fluoresces, or an enzyme.
1. 7. A cloning vector comprising an isolated variant allele of a human orphanin FQ/nociceptin receptor gene and an origin of replication, wherein said variant allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof.
1. 8. A cloning vector comprising an origin of replication and an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human orphanin FQ/nociceptin receptor gene, wherein said variant allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof.

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9. The cloning vector of either of Claims 7 or 8, wherein said cloning vector comprises of *E. coli*, bacteriophages, plasmids, or pUC plasmid derivatives.
10. The cloning vector of Claim 9, wherein bacteriophages further comprise lambda derivatives, plasmids further comprise pBR322 derivatives, and pUC plasmid derivatives further comprise pGEX vectors, or pmal-c, pFLAG.
11. An expression vector comprising an isolated variant allele of a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence having a variation in SEQ ID NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof.
12. An expression vector comprising an isolated nucleic acid molecule selectively hybridizable to an isolated variant allele of a human orphanin FQ/nociceptin receptor gene, wherein said isolated nucleic acid molecule is operatively associated with a promoter, and said variant allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof.
13. The expression vector of either of Claims 11 or 12, wherein said promoter comprises immediate early promoters of hCMV, early promoters of SV40, early promoters of adenovirus, early promoters of vaccinia, early promoters of polyoma, late promoters of SV40, late promoters of adenovirus, late promoters of vaccinia, late promoters of polyoma, the *lac* the *trp* system, the *TAC* system, the *TRC* system, the major operator and promoter regions of phage lambda, control regions of fd coat protein, 3-phosphoglycerate kinase promoter, acid phosphatase promoter, or promoters of yeast α mating factor.
14. A unicellular host transformed or transfected with an expression vector comprising an isolated variant allele of a human orphanin FQ/nociceptin receptor gene operatively associated with a promoter, wherein said variant allele comprises a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation

5 comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T,
6 A804G, C1026T, C1126G, or any combination thereof.

1 15. A unicellular host transformed with an expression vector comprising an isolated nucleic
2 acid molecule selectively hybridizable to an isolated variant allele of a human orphanin
3 FQ/nociceptin receptor gene, wherein said isolated nucleic acid molecule is operatively
4 associated with a promoter, and said variant allele comprises a DNA sequence having at
5 least one variation in SEQ ID NO:1, wherein said at least one variation comprises
6 G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G,
7 C1026T, C1126G, or any combination thereof.

1 16. The unicellular host of either of Claims 14 or 15, wherein said host comprises *E. coli*,
2 Pseudomonas, Bacillus, Streptomyces, yeast, CHO, R1.1, B-W, L-M, COS1, COS7,
3 BSC1, BSC40, BMT10 or SF9 cells.

1 17. A method for determining a susceptibility in a subject to at least one physiological
2 response, condition or disease related to the endogenous opioid system, nociception,
3 neurotransmitter release (including dopamine, GABA, noradrenaline, and serotonin),
4 anxiety and stress, learning, memory and cognition, alcohol self-administration,
5 behavioral sensitization to cocaine, drug addiction, opiate withdrawal and tolerance,
6 food intake, immune function, cardiovascular function, renal function, gastrointestinal
7 function, or motor function, comprising the steps of:
8 a) removing a bodily sample from said subject, wherein said sample comprises a
9 first and second allele comprising a human orphanin FQ/nociceptin receptor
10 gene;
11 b) determining whether said human orphanin FQ/nociceptin receptor gene of said
12 first allele comprises a DNA sequence having at least one variation in SEQ ID
13 NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A,
14 GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any
15 combination thereof, such that the presence of said at least one variation in said
16 human orphanin FQ/nociceptin receptor gene of said first allele is expected to be
17 indicative of the subject's susceptibility to at least one said physiological
18 response, condition or disease relative to the susceptibility to said at least one

said physiological response, condition or disease in a standard.

1 18. The method for determining a susceptibility to at least one addictive disease of Claim 17,
2 further comprising the step of determining whether said human orphanin FQ/nociceptin
3 receptor gene of said second allele comprises a DNA sequence having at least one
4 variation in SEQ ID NO:1, wherein said variation comprises G-46A, GIVS I 135C,
5 GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any
6 combination thereof, such that the presence of said at least one variation in said human
7 orphanin FQ/nociceptin receptor gene of said second allele is expected to be indicative
8 of the subject's susceptibility to said at least one physiological response, condition or
9 disease relative to the susceptibility to said at least one physiological response, condition
10 or disease in said standard.

11 19. The method of either of Claim 19 wherein said at least one addictive disease comprises
12 opioid addiction; cocaine addiction or addiction to other psychostimulants; nicotine
13 addiction; barbituate or sedative hypnotic addiction; anxiolytic addiction; or
14 alcohol addiction.

15 20. A method for determining a susceptibility to pain in a subject relative to a susceptibility
16 of pain in a standard, wherein the method comprises the steps of:
17 a) removing a bodily sample from said subject, wherein said sample comprises a
18 first and second allele comprising a human orphanin FQ/nociceptin receptor
19 gene;
20 b) determining whether said human orphanin FQ/nociceptin receptor gene of said
21 first allele comprises a DNA sequence having at least one variation in SEQ ID
22 NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A,
23 GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any
24 combination thereof, such that the presence of said at least one variation in said
25 human orphanin FQ/nociceptin receptor gene of said first allele is expected to be
26 indicative of susceptibility to pain in said subject relative to susceptibility to
27 pain in said standard, wherein said first allele of said standard comprises a
28 human orphanin FQ/nociceptin receptor gene comprising a DNA sequence of
29 SEQ ID NO:1.

21. The method of Claim 20 for determining a susceptibility to pain in a subject, further comprising the step of determining whether said second allele of said bodily sample comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility of pain in said standard, wherein said second allele of said standard comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence of SEQ ID NO:1.

22. A method for determining a therapeutically effective amount of pain reliever to administer to a subject in order to induce analgesia in said subject relative to a therapeutically effective amount of pain reliever to administer to a standard in order to induce analgesia in said standard, wherein the method comprises determining a susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein susceptibility to pain in said subject is expected to be indicative of said therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject relative to said therapeutically effective amount of pain reliever to administer to said standard to induce analgesia in said standard.

23. The method of Claim 22 for determining a therapeutically effective amount of pain reliever to administer to said subject, wherein determining susceptibility to pain in said subject comprises the steps of:

- removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human orphanin FQ/nociceptin receptor gene; and
- determining whether said first allele comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof, wherein the presence of said at least one variation in

12 said human orphanin FQ/nociceptin receptor gene of said first allele is expected
13 to be indicative of the subject's susceptibility to pain relative to said to
14 susceptibility of pain in said standard, wherein said first allele of said standard
15 comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA
16 sequence of SEQ ID NO:1, such that said therapeutically effective amount of
17 pain reliever to administer to the subject in order to induce analgesia is related to
18 said susceptibility to pain in said subject relative to susceptibility to pain in said
19 standard.

24. The method of Claim 23, wherein determining susceptibility to pain in said subject relative to susceptibility to pain in said standard further comprises the step of determining whether said second allele of said bodily sample from said subject comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said at least one variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof, such that the presence of said at least one variation in said second allele is expected to be indicative of susceptibility to pain in said subject relative to susceptibility to pain in said standard, wherein said second allele of said standard comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence of SEQ ID NO:1, and the therapeutically effective amount of pain reliever to administer to said subject to induce analgesia in said subject is related to the presence of said at least one variation in said human orphanin FQ/nociceptin receptor gene of said second allele of said bodily sample from said subject.

25. A method for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from at least one addictive disease to treat the at least one addictive disease in said subject relative to a therapeutically effective amount of therapeutic agent to administer to a standard suffering from the at least one addictive disease to treat the at least one addictive disease in said standard, wherein the method comprises the steps of:

- removing a bodily sample from said subject, wherein said sample comprises a first and second allele comprising a human orphanin FQ/nociceptin receptor gene; and

b) determining whether said first allele comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof,

wherein the presence of said at least one variation in said human orphanin FQ/nociceptin receptor gene of said first allele is expected to be indicative of the therapeutically effective amount of said therapeutic agent to administer to the subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said first allele of said standard comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence of SEQ ID NO:1.

26. The method of Claim 25 for determining a therapeutically effective amount of therapeutic agent to administer to a subject suffering from said at least one addictive disease to treat said at least one addictive disease, relative to said therapeutically effective amount of said therapeutic agent administered to said standard suffering from said at least one addictive disease to treat said at least one addictive disease in said standard, further comprising the step of determining whether said second allele of said bodily sample from said subject comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence having at least one variation in SEQ ID NO:1, wherein said variation comprises G-46A, GIVS I 135C, GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G, or any combination thereof, such that the presence of said at least one variation in said second allele related to said therapeutically effective amount of said therapeutic agent administered to said subject to treat said at least one addictive disease in said subject relative to said therapeutically effective amount of said therapeutic agent to administer to said standard to treat said at least one addictive disease in said standard, wherein said second allele of said standard comprises a human orphanin FQ/nociceptin receptor gene comprising a DNA sequence of SEQ ID NO:1.

27. The method of either of Claims 25 or 26, wherein said at least one addictive disease

2 comprises opioid addiction; cocaine addiction or addiction to other psychostimulants;
3 nicotine addiction; barbiturate or sedative hypnotic addiction; anxiolytic addiction; or
4 alcohol addiction.

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2 28. A commercial test kit may for determining the presence of at least one variation in a
3 human orphanin FQ/nociceptin receptor gene of an allele in a bodily sample taken from
4 a subject, wherein the commercial test kit comprises:
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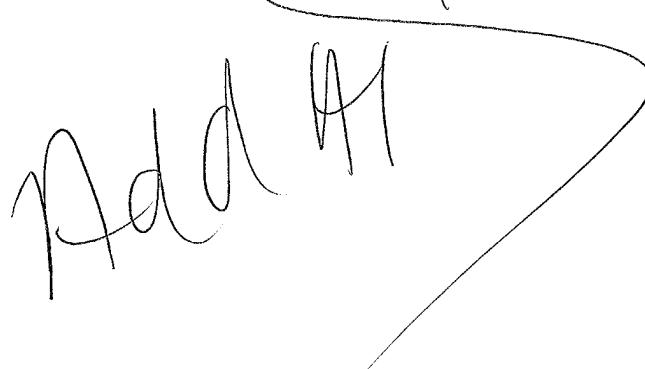
6 a) PCR oligonucleotide primers suitable for detection of an allele comprising a
7 human orphanin FQ/nociceptin receptor gene comprising a DNA sequence
8 having at least one variation in SEQ ID NO:1 comprising G-46A, GIVS I 135C,
9 GIVS I 250A, GIVS I 251A, C510T, CIVS III 67T, A804G, C1026T, C1126G,
10 or any combination thereof;
11 b) other reagents; and
12 c) directions for use of the kit.

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14 29. A nucleic acid comprising an intron of the human orphanin FQ/nociceptin receptor gene
15 as set forth in SEQ ID No:2.

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17 30. A nucleic acid as set forth in SEQ ID No:2.

A handwritten signature in black ink, appearing to read "Add H", is written over a large, faint, curved arrow pointing downwards and to the right.